

CEA Study Evaluation Guidelines

Cost-Effectiveness Analysis (CEA) Studies Funding Program

Purpose and Background

As part of its Prioritization and Scientific Quality Initiatives, the Clinical Trials Working Group (CTWG) of NCI recommended establishing a funding mechanism and prioritization process for essential correlative biomarker, imaging, and QOL studies that are incorporated into the fundamental design of a clinical trial. In 2011, Cost Effectiveness Analysis (CEA) was added to this funding program. The objective is to ensure that the most important CEA studies can be conducted in a timely manner in association with NCI-sponsored clinical trials.

Cost-Effectiveness Analysis (CEA) provides useful information to help health care payers manage the use of costly medical technologies in order to maximize the health of their patient populations when facing constrained budgets, and to clinicians and patients to help guide treatment decisions based on CEA's unique endpoints, perspectives (e.g., societal, clinical, or third-party), and time horizon (e.g., within trial or long-term survivorship). To be most useful to decision-makers, CEA of new cancer therapies must have maximal feasibility, be timely, and have high internal validity.

Conducting a CEA alongside a clinical trial can achieve these goals and also offers the benefit of efficiency by utilizing the existing structure of clinical trials to collect additional data for the economic analysis. It is not required that a CEA proposal be included with each clinical trial concept submitted. However, in some instances the addition of CEA may be recommended during evaluation review of the clinical trial concept.

The primary purpose of this funding mechanism is to support CEA studies that are paired with phase 3 clinical trials that have a comparator arm, conducted by the Cooperative Groups (CG's) and Community Cancer Oncology Program (CCOP) Research Bases.

Requirements and Definition

Eligible trial types are:

- Randomized Phase 3 clinical trial concepts with a comparator arm

BIQSFP proposals for funding of CEA study applications **must be submitted after parent concept approval and must be received within four months** of notification of parent concept approval.

CEA Studies

The CEA evaluation criteria are intended to help guide the selection of cancer clinical trials that warrant additional funds for a CEA. The CEA study should be a secondary endpoint of the parent concept. NCI's Scientific Steering Committees (SSCs) evaluate CEA proposals paired with clinical trial concepts through their concept evaluation and prioritization process. SSCs will make use of ad hoc CEA expert(s), including resources available at the NCI, to evaluate CEA proposals included in clinical trial concepts.

Criteria for Review of CEA Proposals

Researchers should consider pairing a CEA proposal to phase 3 clinical trials when the following conditions are met:

- The results of a phase 3 clinical trial are expected to substantially influence clinical practice.
- The cost-effectiveness study would be of high impact judged by substantial budget implications for health care systems, either in terms of overall cost savings or added costs to the system.
- It is feasible to conduct a high quality CEA as part of the clinical trial. Specific issues to consider include:
 - The comparator arm should be relevant to current clinical practice.
 - The trial should be of sufficient duration, with respect to follow-up of patient outcomes, that consequences of interest to economic evaluation can be captured either directly or through modeling.
 - There is reasonable statistical power for the key cost-effectiveness analysis.
- Because of high cost of the experimental treatment, there is a reasonable degree of uncertainty regarding the outcome of the CEA even if the clinical outcome favors the experimental treatment.

Modeling is a pivotal part of the CEA proposal. CEA proposals should describe the general type of model that will be used. If a model is to be developed, the expertise of model developer, timeline for model development, calibration, and validation (if relevant) must be included in the proposal. This may include but not be limited to all model inputs that are needed and sources for these inputs, what provisions need to be made to document model structure, assumptions, data inputs, parameter estimation, intermediate and final outputs so that replication of the CEA would be possible by an external analyst.

CEA proposals included in phase 3 clinical trial concepts should be developed by NCTN/CCOP Networks/NCORPs. When NCTN/CCOP Networks/NCORPs choose to submit a CEA proposal, it must be submitted after parent concept approval but must be received within four months (16 weeks) of their notification of the parent concept approval.

Cost-Effectiveness Analysis Proposal Package/Budget Submission

The BIQSFP CEA Proposal Package should include a completed *Study Checklist for Randomized Phase 3 Clinical Trials with a Comparator Arm and Cost-Effectiveness Analysis (CEA) Component* (see below). The CEA application should include a response to each of the elements. This section is not to exceed **eight (8) pages**.

The CEA Proposal Package must also include a budget at the time of submission that clearly details the Direct and Indirect costs of the requested funding. The budget for the project should use the **standard PHS 398 budget form (<http://grants.nih.gov/grants/funding/phs398/phs398.html>)** along with a narrative justifying each requested cost. The Budget packet must include a completed NIH biosketch form for each study PI. Form SF424 can be found at: <http://grants.nih.gov/grants/funding/424/index.htm#format>. Additional information on the new biosketch requirements can be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-024.html>.

Biomarker, Imaging, & QOL Studies Funding Program (BIQSFP)

'15 Study Checklist for Randomized Phase 3 Clinical Trials with a Comparator Arm and Cost-Effectiveness Analysis (CEA) Component

INSTRUCTIONS: Please submit a response to each of the criteria below and complete one Study Checklist for each CEA endpoint. The Proposal Package must also include a budget at the time of submission that clearly details the Direct and Indirect costs of the requested funding. The budget for the project should use the standard PHS 398 budget form (<http://grants.nih.gov/grants/funding/phs398/phs398.html>) along with a narrative justifying each requested cost. The Budget packet must include a completed NIH biosketch form for each study PI. Form SF424 can be found at: <http://grants.nih.gov/grants/funding/424/index.htm#format>. Additional information on the new biosketch requirements can be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-024.html>.

NOTE: One-time INTEGRATED CEA study applications must be submitted after parent concept approval and must be received within four months of notification of parent concept approval. Subsequent NCI prioritization and approval for funding will be decided by CTROC after evaluation of the INTEGRATED study(s) by the respective SSC.

1. Explain why it is necessary to conduct this CEA alongside the parent clinical trial. For example, explain why an independent modeling study conducted during or after the clinical trial is completed is not feasible and/or why it would be of lesser value in informing clinical practice and/or policy compared to a CEA conducted alongside the parent clinical trial.
2. Describe and justify the perspective of the CEA.
3. Explain the situations in which the outcomes of the clinical trial could substantially change clinical practice.
4. Describe the potential implication(s) of different outcomes of the trial on overall costs to the health care system, in terms of costs saved or costs added.
5. Briefly describe and justify the CEA study in terms of:
 - A. Trial population (in relationship to treatment population in community practice)
 - B. Intervention(s) and control therapy selected for the CEA
 - C. Question or hypothesis posed
 - D. Measure(s) of outcome for the CEA
 - E. Method of estimating costs
 - F. Modeling approach proposed (if appropriate; e.g., decision tree, Markov, micro-simulation, etc. Provide sources of documentation if using an existing model. If a model is to be developed, the expertise of model developer, timeline for model development, calibration, and validation (if relevant) must be included in the proposal. This may include but not be limited to all model inputs that are needed and sources for these inputs, what provisions need to be made to document model structure, assumptions, data inputs, parameter estimation, intermediate and final outputs so that replication of the CEA would be possible by an external analyst.)
 - G. Approach to characterizing uncertainty analysis

- H. The time horizon and discount rates of the CEA. If the time horizon of the CEA exceeds that of the trial, describe the extrapolation or modeling approach that will be used.
6. Describe all data elements that will be collected for the CEA. This description should include:
- A. A description of data elements that will already be collected as part of the protocol of the parent study and which additional data elements will need to be collected.
A description of the data instrument development and validation process for new data elements.
 - B. A description of resources and personnel required for data collection and how the added data collection is consistent with the intended protocol of the parent study, i.e. is it logistically feasible and will not create an unreasonable additional burden.
 - C. A description of any sources of data elements external to the parent protocol (e.g. linked or unlinked administrative data). If relevant describe external data sources and methods for obtaining estimates of unit cost. Provide information supporting whether unit cost estimates are relevant, consistent and valid.
7. Provide a power analysis to indicate that the sample sizes for health outcomes and economic data elements are sufficient to result in confidence intervals around the cost effectiveness ratio that render the results of the CEA useful to decision makers.
8. Describe any threats to the external validity of the study in relation to community practice.

3/10,3/11,3/12,1/13,11/13,12/14

**Please complete and return the attached
CEA STUDY EVALUATION TEMPLATE.**

Thank you.